

## R E M A R K S

Claims 1-53 were filed in the original application. Claims 1-53 were cancelled in response to a restriction requirement and new claims 54-82 were added. In the present response, claims 54-82 are cancelled and new claims 83-94 are added. Support for the new claims is found through the specification, including, for example (references made to the published application 20040191812):

An embodiment of the current invention comprises a method of making RNA. This method comprises: (a) obtaining a N4 virion RNA polymerase (i.e. the polypeptide); (b) obtaining DNA wherein the DNA preferably contains a N4 virion RNA polymerase promoter sequence; (c) admixing the RNA polymerase and the DNA; and (d) culturing the RNA polymerase and the DNA under conditions effective to allow RNA synthesis. (paragraph 25)

A number of template dependent processes are available to amplify the marker sequences present in a given template sample. (paragraph 122)

Methods based on ligation of two (or more) oligonucleotides in the presence of nucleic acid having the sequence of the resulting "di-oligonucleotide," thereby amplifying the di-oligonucleotide, may also be used in the amplification step of the present invention. (paragraph 133)

Controlled trypsin proteolysis of vRNAP was performed, followed by catalytic autolabeling and analysis on SDS-PAGE (FIG. 3A). Initially, three proteolytic fragments are generated, of which the smaller two are catalytically active. Upon further incubation with trypsin, a single stable, transcriptionally active product approximately 1,100 amino acids in length remains. N-terminal sequencing of the three initial proteolytic fragments (FIG. 3B) indicated that the stable active polypeptide (mini-vRNAP) corresponds to the middle 1/3 of vRNAP, the region containing the three motifs described above (FIG. 2A, SEQ ID NOS:3-4). (paragraph 603)

The invention provides methods of using a novel N4 virion RNA polymerase (vRNAP), a

mini-vRNA polymerase, and compositions and related kits. The novel polymerases are described by an isolated nucleic acid comprising a region encoding a polypeptide having the amino sequence set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:15. The nucleic acid may comprise the nucleic acid sequence of SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, or SEQ ID NO:14. In preferred embodiments of the invention, the RNA polymerase comprises a transcriptionally active 1,106-amino acid domain of the N4 vRNAP (herein designated "mini-vRNAP"), which corresponds to amino acids 998-2103 of N4 vRNAP, as described herein. The vRNAP and mini-vRNA polymerase transcribe nucleic acid operatively linked to an N4 promoter such as a P2 promoter of SEQ ID NO:16, SEQ ID NO:19, SEQ ID NO:27, SEQ ID NO:28 or SEQ ID NO:29. The promoter of SEQ ID NO:16 or SEQ ID NO:28 is preferred.

(paragraph 21)

In another aspect, the current invention can use a polypeptide encoded by an isolated nucleic acid comprising a region encoding at least 6 contiguous amino acids of SEQ ID NO:2, wherein the polypeptide has RNA polymerase activity under appropriate reaction conditions. It is preferred that this polypeptide comprises at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 75, 100, 150, 200, 250, 300, 400, 600, 800, 1000 or more contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:15. The encoded polypeptide may have at least one hexahistidine tag or other tag, or the encoded polypeptide may lack a tag. The polypeptide may be a mutant of the peptide found in SEQ ID NO:2 or SEQ ID NO:4, such as an enzyme possessing an amino acid substitution at position Y678.

(paragraph 24)

4) The method of claim 1, wherein the method is used for detecting an analyte in a sample, wherein the target nucleic acid sequence comprises a target sequence tag that is joined to an analyte-binding substance, the method further comprising prior to step (a) contacting the analyte-binding substance with the analyte to form a specific binding pair and separating the specific binding pair from analyte-binding substance molecules that are not bound to the analyte.

5) The method of claim 4, wherein the analyte is selected from the group consisting of a biochemical molecule, a biopolymer, a protein, a glycoprotein, a lipoprotein, an enzyme, a hormone, a biochemical metabolite, a receptor, an antigen, an antibody, a nucleic acid, a DNA molecule, an RNA molecule, a polysaccharide and a lipid.

6) The method of claim 4, wherein the analyte-binding substance is selected from the group consisting of a nucleic acid, a polynucleotide, an oligonucleotide, a segment of a nucleic acid or polynucleotide, a DNA molecule, an RNA molecule, a molecule

comprising both DNA and RNA mononucleotides, modified DNA mononucleotides, a molecule obtained by a method termed "SELEX", a nucleic acid molecule having an affinity for protein molecules, a polynucleotide molecule having an affinity for protein molecules, an operator, a promoter, an origin of replication, a ribosomal nucleic acid sequence, a sequence recognized by steroid hormone-receptor complexes, a peptide nucleic acid (PNA), a nucleic acid and a PNA, a molecule prepared by using a combinatorial library of randomized peptide nucleic acids, an oligonucleotide or polynucleotide with a modified backbone that is not an amino acid, a lectin, a receptor for a hormone, a hormone, and an enzyme inhibitor.

(Claims 4 through 6 as filed)

Applicants note that all amendments and cancellations of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and are made solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),<sup>1</sup> and without waiving the right to prosecute the amended Claims (or similar Claims) in the future.

## **I. Priority Claim**

The Examiner has not accorded the claims with the priority date of the parent applications. This denial of priority is moot in view of Applicants cancellation of the claims. At least new claims 83-87 and 93-94 are entitled to priority to the parent applications. For example, U.S. Appl. Ser. No. 10/153,219, filed May 22, 2002 and claiming priority to a provisional application filed May 22, 2001, contains the following paragraphs (referenced with respect to the published application 20030096349):

An embodiment of the current invention comprises a method of making RNA. This method comprises: (a) obtaining a N4 virion RNA polymerase (i.e. the polypeptide); (b) obtaining DNA wherein the DNA preferably contains a N4 virion RNA polymerase promoter sequence; (c) admixing the RNA polymerase and the DNA; and (d) culturing the RNA polymerase and the DNA under conditions effective to allow RNA synthesis. (paragraph 15)

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<sup>1</sup> 65 Fed. Reg. 54603 (Sept. 8, 2000).

A number of template dependent processes are available to amplify the marker sequences present in a given template sample.  
(paragraph 98)

Methods based on ligation of two (or more) oligonucleotides in the presence of nucleic acid having the sequence of the resulting "di-oligonucleotide," thereby amplifying the di-oligonucleotide, may also be used in the amplification step of the present invention.  
(paragraph 109)

Upon further incubation with trypsin, a single stable, transcriptionally active product approximately 1,100 amino acids in length remains. N-terminal sequencing of the three initial proteolytic fragments (FIG. 3B) indicated that the stable active polypeptide (mini-vRNAP) corresponds to the middle 1/3 of vRNAP, the region containing the three motifs described above (FIG. 2A, SEQ ID NOS:3-4).  
(paragraph 275)

The invention provides a novel N4 virion RNA polymerase (vRNAP) and a mini-vRNA polymerase and method of use thereof. The novel polymerases are described by an isolated nucleic acid comprising a region encoding a polypeptide having the amino sequence set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:15. The nucleic acid may comprise the nucleic acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7 or SEQ ID NO:14. The vRNAP and mini-vRNA polymerase transcribe nucleic acid operatively linked to an N4 promoter such as a P2 promoter of SEQ ID NO:16, SEQ ID NO:19, SEQ ID NO:27, SEQ ID NO:28 or SEQ ID NO:29. The promoter of SEQ ID NO:16 or SEQ ID NO:28 is preferred.  
(paragraph 10)

Yet another aspect of the current invention comprises an isolated nucleic acid comprising a region encoding a polypeptide comprising at least 6 contiguous amino acids of SEQ ID NO:2, wherein the polypeptide has RNA polymerase activity under appropriate reaction conditions. It is preferred that this polypeptide comprises at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 75, 100, 150, 200, 250, 300, 400, 600, 800, 1000 or more contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:15. The encoded polypeptide may have at least one hexahistidine tag or other tag. The polypeptide may be a mutant of the peptide found in SEQ ID NO:2 or SEQ ID NO:4, such as an enzyme possessing an amino acid substitution at position Y678.  
(paragraph 14)

## **II. Oath/Declaration**

The oath/declaration has been objected to as containing an un-initialed alteration. A new oath/declaration is provided herewith.

**III. Embedded hyperlinks**

The specification has been objected to for containing embedded hyperlinks. Applicants have amended the specification to delete the “http/www.”

The abstracts have been objected to for missing a period. Applicants have provided a new abstract, adding the period.

**IV. The claims are definite**

The Examiner has rejected claims 54-80 on various grounds related to indefiniteness. Applicants respectfully disagree. However, Applicants believe the rejection is moot in view of the cancellation of claims 54-80.

**V. The claims are non-obvious**

The Examiner has rejected claims 54-80 on various grounds related to obviousness. Applicants respectfully disagree. However, Applicants believe the rejection is moot in view of the cancellation of claims 54-80. With respect to the new claims, Applicants note that the primary reference Wenz et al. (U.S. 2003/0119004) has a filing date of December 5, 2001. The present claims have a priority date of May 22, 2001. Thus, Wenz et al. is not prior art.

With respect to claims 88-92, Applicants note that Wenz, alone or in combination with the other references, does not teach or suggest:

a target sequence tag that is joined to an analyte-binding substance and the method is used for detecting an analyte to which the analyte-binding substance binds, wherein, prior to performing step (b), the method additionally comprises the steps of: obtaining the analyte-binding substance to which the target sequence tag is joined; contacting the analyte-binding substance to which the target sequence tag is joined with the analyte to form a specific binding pair; removing the analyte-binding substance molecules that are not bound to the analyte from the specific binding pair; and providing the specific binding pair from which the analyte-binding substance molecules that are not bound to the analyte have been removed.

In view of the above, Applicants request that the prior art rejection be withdrawn.

**VI. Conclusion**

If the Examiner wishes to discuss this case, Applicants encourage the Examiner to call the undersigned at 608-218-6900 at the Examiner's convenience.

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